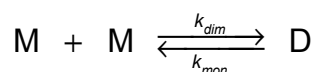


Supplementary Material:

A Kinetic Study of Domain Swapping in Protein L

For a homodimerization reaction of a protein according to the scheme



k_{dim} and k_{mon} are the rate constants for dimerization and monomerization, and the dissociation constant of the homodimer D is given by

$$(1) \quad K_d = \frac{k_{mon}}{k_{dim}}$$

The rate equations for the forward and backward reactions are:

$$(2) \quad \frac{d[M]}{dt} = -k_{dim}[M]^2 + 2k_{mon}[D]$$

$$(3) \quad \frac{d[D]}{dt} = k_{dim}[M]^2 - k_{mon}[D]$$

where [M] and [D] are the concentrations of the monomeric and the dimeric state.

For a total concentration of protein, c_0 , with

$$(4) \quad c_0 = [M] + 2 \cdot [D]$$

[M] is given by

$$(5) \quad [M] = c_0 - 2 \cdot [D]$$

Using equations (1) and (5) the rate equation (3) can be recast to

$$(6) \quad \frac{d[D]}{dt} = k_{dim} (c_0 - 2 \cdot [D])^2 - k_{dim} \cdot K_d \cdot [D]$$

which can be written as

$$(7) \quad \frac{d[D]}{-\left([D]^2 + [D] \cdot \left(-c_0 - \frac{K_d}{4}\right) + \frac{1}{4}(c_0)^2\right)} = -4k_{dim} dt$$

expansion of the left hand side into partial fractions using

$$(8) \quad \frac{d[D]}{-([D] - \lambda_1) \cdot ([D] - \lambda_2)} = -4k_{dim} dt$$

and

$$(9) \quad \lambda_{1/2} = \frac{1}{2} \left(\frac{k_{mon}}{4k_{dim}} + c_0 \right) \pm \sqrt{\frac{1}{4} \left(\frac{k_{mon}}{4k_{dim}} + c_0 \right)^2 - \frac{1}{4}(c_0)^2}$$

yields

$$(10) \quad -\frac{d[D]}{(\lambda_1 - \lambda_2)([D] - \lambda_1)} + \frac{d[D]}{(\lambda_1 - \lambda_2)([D] - \lambda_2)} = -4k_{dim} dt$$

Integration of equation (10) on both sides gives

$$(11) \quad \frac{1}{(\lambda_1 - \lambda_2)} \cdot \ln \left(\frac{[D] - \lambda_2}{[D] - \lambda_1} \right) = -4k_{dim} t + const$$

Assuming $[D] = 0$ at $t = 0$ (*i.e.* starting the reaction from the monomer) to calculate

$$(12) \quad const = \frac{1}{(\lambda_1 - \lambda_2)} \cdot \ln \left(\frac{\lambda_2}{\lambda_1} \right)$$

yields the time course of the concentrations of homodimer, $[D(t)]$, and monomer, $[M(t)]$, as

$$(13) \quad [D(t)] = \frac{\lambda_1 \lambda_2 (1 - \exp(-4k_{dim}(\lambda_1 - \lambda_2) \cdot t))}{\lambda_1 - \lambda_2 \exp(-4k_{dim}(\lambda_1 - \lambda_2) \cdot t)}$$

$$(14) \quad [M(t)] = c_0 - 2 \frac{\lambda_1 \lambda_2 (1 - \exp(-4k_{dim}(\lambda_1 - \lambda_2) \cdot t))}{\lambda_1 - \lambda_2 \exp(-4k_{dim}(\lambda_1 - \lambda_2) \cdot t)}$$

Populations of M and D are obtained by dividing equations (13) and (14) by c_0 .